

Applicants respectfully traverse the rejection. When applying 35 U.S.C. § 103, the Examiner is required to adhere to the following tenets of patent law: (1) The claimed invention must be considered as a whole; (2) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination; (3) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and (4) Reasonable expectation of success is the standard with which obviousness is determined. (MPEP, 2141.01). In addition, all the claim limitations must be taught or suggested by the prior art to establish a *prima facie* case of obviousness of a claimed invention. In re Royka, 490 F.2d 981, 180 USPQ 580 (CCPA 1974).

The instant invention claims methods for inducing the regression of dermal tumors or for treating infections of the respiratory tract in humans by administering a bacterial product comprising heat-killed, terminally sterilized *P. acnes*.

Adlam reports that intravenous injection of formalin-inactivated *P. acnes* stimulates the lympho-reticular system in mice.

Howard reports that inactivated *P. acnes* augments the B cell response to the thymus-independent antigen SIII in mice.

Evans provides that intravenous injection of inactivated *P. acnes* can be used as an adjunct to conventional therapy to increase the rate of recovery from equine respiratory diseases.

Fujiwara describes that injection of *P. acnes* reduces tumor metastasis, but not primary tumor growth in mice.

Megid et al. authorized three references [Megid et al. Vaccine 17 (1999), 2446 (Megid I); Megid et al. Rev. Inst. Med. trop. S. Paulo 41 (1999), 107 (Megid II); and Megid et al. Comparative Immunology, Microbiology & Infectious Diseases 23 (2000), 91 (Megid III)].

Megid I demonstrates that administration of *P. acnes* as an adjuvant for an anti-rabies vaccine may affect humoral and cellular response, but does not reveal any encouraging results. Megid II and III, on the other hand, show that *P. acnes* treatment improves the survival rate of mice infected with rabies virus.

Neifeld describes that preoperative intratumoral injection of *P. acnes* and postoperative subcutaneous injection of *P. acnes* are ineffective when used as an adjuvant to surgery for primary cancers of the oral cavity, pharynx, and larynx.

Applicants respectfully submit that the cited references do not teach nor suggest using *P. acnes* as a treatment for dermal tumor or respiratory tract infections in humans. As described above, the Adlam and Howard references generally describe the stimulating effect of *P. acnes* on the immune system. The references, however, provide no evidence that the immune stimulation would lead to an effective treatment for a particular disease. It was well known in the art at the time of the invention that an immune stimulant may not necessarily have antineoplastic and/or antiviral effect, and that an immune stimulant that is effective in treating one disease may not be effective in treating another disease. For example, Megid II shows that administration of *P. acnes* improves the survival rate of mice infected with rabies virus, but Megid I shows the treatment is not effective as an adjuvant for an anti-rabies vaccine in mice. Similarly, while Fujiwara describes that injection of *P. acnes* reduces the metastasis of plasmacytoma, Neifeld demonstrates that treatment with *P. acnes* is ineffective for primary cancers of the oral cavity, pharynx, and larynx. Therefore, Adlam, Howard, Megid I-III, Fujiwar, and Neifeld, when considered individually or in combination, do not make it obvious to one skilled in the art that *P. acnes* can be used to treat any tumor or viral infections.

With regard to respiratory tract infections, only Evans provides that *P. acnes* can be used as **an adjunct to conventional therapy** to increase the rate of recovery from equine respiratory diseases. Evans does not teach or suggest using *P. acnes* **alone** as a treatment for equine respiratory diseases.

Furthermore, none of the cited references teaches or suggests the use of terminally sterilized *P. acnes* for the treatment of neoplastic or viral diseases. Among the eight references, only Adlam and Fujiwara disclose the inactivation procedure for *P. acnes* (formalin in Adlam and heat in Fujiwara). None of the references addresses the effect of inactivation procedure on the immune modulator activity of *P. acnes*. Therefore, the references provide no motivation to one skilled in the art to modify the inactivation procedure by terminal sterilization.

In addition, the combination of the cited references do not support a reasonable expectation of success. Out of the eight cited references, Adlam and Howard do not show any therapeutic results. Megid I and Neifeld demonstrate that *P. acnes* treatment is not effective for rabies virus and a number of primary cancers. Fujiwara provides that the *P. acnes* treatment reduces tumor metastasis, but not primary tumor growth. Only Magid II, Magid III and Evans report some positive result in using *P. acnes* for treating rabies virus (Magid II and III) and as an adjunct to conventional therapy for equine respiratory diseases (Evans). Taken together, Applicants respectfully submit these references do not support the Office Action's conclusion that "[t]he huge breadth of teachings in the art give the skilled artisan a reasonable expectation of success to treat neoplastic or viral maladies."

In summary, Applicants respectfully submit that the Office Action has failed to establish a *prima facie* case of obviousness. Withdraw of the 35 U.S.C. 103 rejections is respectfully requested.

## II. Request for Interview

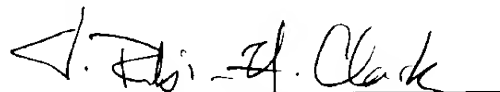
In order to expedite prosecution, Applicants respectfully request a personal interview with the Examiner to discuss the application. The Examiner is invited to telephone the undersigned attorney to set up a time for the interview.

### CONCLUSION

In view of the above remarks, it is respectfully submitted that this application is in condition for allowance and such action is earnestly solicited.

Respectfully submitted,

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